

University of Groningen

How do you feel today?

Roppolo, Mattia

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2015

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Roppolo, M. (2015). *How do you feel today? The use of a Dynamic Systems approach in the conceptualization and analysis of Health Related Quality of Life in the older adults*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

CHAPTER 1

INTRODUCTION

1. Preface

This thesis is inspired by the experiences I had working at a residential care facility while studying for my Master's Degree. My work consisted of physical rehabilitation of the older adults who lived there. Despite all my efforts to customize the activities and to advance progression and differentiation of the stimuli proposed on a daily basis, results varied greatly. Subjects often responded very well to some series of exercises one day, while they behaved opposite the day after. Other times, hard-won progress over a long period of time was completely and instantly reset by external influences that were not directly attributable to the physical sphere. Fortunately, however, sometimes individuals who had in previous months shown no progress at all, showed a sudden increase in their physical health status, without any clear reason. I could not find explanations for these changes and "strange" patterns of development, and they raised questions that I tried to solve with the work and the articles presented in this thesis.

The same situation occurred when I started my research. During the first years, I was involved in a great Italian project called ACT ON AGEING, developed at the Department of Psychology at the University of Torino by Professor Silvia Ciairano. ACT ON AGEING aimed to increase the physical and cognitive health status in a large sample of older adults through the implementation of different interventions. Despite the good and general success of the project, results were heterogeneous in this instance as well, with some participants improving greatly, while others showed no change or even experienced worsening health conditions.

My involvement in the ACT ON AGEING project presented me with the opportunity to find answers to the following questions: why did our interventions, which are specific, scientifically valid and supported by literature, not produce consistent results in most of the participants? Why did similar stimuli on different days create different outcomes? How could external events change or reverse trends that were built week after week?

Fortunately, some research helped me find at least one way to answer my questions. I started reading books that dealt with complex systems from a philosophical, biological, economical point of view, and even though the topics were so far removed from my own field of interest, I found page after page of possible similarities between these disciplines and my specific and concrete questions. I learned that complex and Dynamic Systems were also studied and developed in Psychology. Specifically, one of the most important research groups in Dynamic Systems is the one at the Department of Developmental Psychology at the University of Groningen. This was particularly fortuitous

Chapter 1 - Introduction

because my late PhD promoter Prof. Silvia Ciairano defended her PhD thesis at the Groningen University, and since she had an “international soul” (something she had passed on to her students) she suggested that I contact Prof. Saskia Kunnen and Prof. Paul van Geert in order to discuss my doubts and possible solutions.

Three years later, I am not sure whether the results I have found and the route I have walked have brought me to the final solution of my initial questions, but one thing is for certain: I learned a lot about human development and I acquired a “new pair of glasses” that helped me look at the world in a different way.

Il senso della ricerca sta nel cammino fatto e non nella meta; il fine del viaggiare è il viaggiare stesso e non l'arrivare.

(TizianoTerzani, 2006)

The sense of research is done in the journey, not the destination; the end of the travel is the travel itself and not the arrival.

(TizianoTerzani, 2006)

2. Demographic changes

2.1 The old Europe

The ageing of European society is well described and projected by the statistics of the World Health Organization and Eurostat. These statistics show that the general population is expected to face a slight increase between 2008 and 2060 (2.1%), and the aged population (65 years and over) is expected to show a huge growth rate in the same period (80%) (Eurostat, 2012). As a consequence, 33% of the European population is expected to be composed of aged people in 2060 (Giannakouris, 2008).

The decrease of the birth and fertility rate together with the increase of the number of older adults will generate a change in the population pyramid (Pollack, 2005): the base of the pyramid (infants and children) will get smaller, while the top will get substantially larger (Giannakouris, 2008).

If we imagine the European population as a pie, we can see that the slice of the older adults (over 65 years) is gradually becoming the largest slice. Eurostat (2012) reports that in 2000, 15.6% (min. 5.4% max. 18.1%) of the population consisted of people over age 65. Over the course of ten years, this percentage increased steadily until in 2010 it had risen to 17.4% (min. 7% and max. 20.7%). A similar trend can be seen for the people aged 80 and over.

A relevant aspect of this change in the population is the so-called old-age dependency ratio. The old-age dependency ratio is defined as the rate between the number of economically inactive older adults and the number of persons of working age (Eurostat, 2012). Longitudinal European data from 1990 to 2010 (Eurostat, 2012) show an increase of 5.3% of this indicator (20.6% in 1990, 23.2 % in 2000, and 25.9% in 2010). This means that in 1990 in the European zone, for each inactive aged person, there were five who were economically active. In 2010, this ratio was 1:4. The Eurostat projections (Giannakouris, 2008) reveal a steady increase of this rate until 2060, when the rate is estimated to be 52.5% (this means that for each economically inactive aged person, there will be two economically active persons). These trends are relevant for both national and European governments, because social and economic adaptations will be necessary in answer to the new demands of the population.

2.2 Theories of ageing

The demographic analysis has shown that the European population is growing old rapidly. Next, we will focus on the age-related process, in order to understand what happens during the later part of life.

The current theories assume that age-related development is a complex and multifactorial process (Weinert & Timiras, 2003) in which three components play a role: the internal factor (i.e., genetics), the external factor (i.e., environment), and the stochastic factor (i.e., random events). These factors interact with each other to cause the ageing process. Theories that seek to understand the mechanism behind the ageing process aim to define why and how a person ages. The main theories of ageing are: (i) the evolutionary theory, which states that ageing is due to a lack in selection; (ii) the molecular theory, which states that the changes in genes expression are the main cause of senescence; (iii) the cellular theory, which states that senescence as a process is related to the cellular limits in replications, with a consequent alteration in the cells' physiology; (iv) systemic theories, which focus on the incapacity of the whole organism to maintain and control organs and systems and the inability to communicate and adapt environmental requests (Franceschi et al., 2000; Kirkwood, 2002; Kirkwood & Kowald, 1997; Weinert & Timiras, 2003). These theories will not be extensively discussed here, but it is important to note that they are not mutually exclusive and can act simultaneously.

In general, we can say that the ageing process is characterized by a loss of homeostasis (defined as the propriety that a system has to maintain its internal environment's stability) and a reduced ability to respond to the external requests (Weinert & Timiras, 2003) that causes an increase in incidences of disease and finally death. These descriptions make it clear that ageing is a period of change that involves the whole person.

2.3 Life expectancy

In order to understand the demographic change and its consequences, it is important and necessary to consider the most used and common population index, the Life Expectancy (LE), which is the expected numbers of years remaining at a certain age.

As previously described, the population is getting older. This demographic change is due to improvements in living conditions and medicine and medical care amelioration, with a decline in deaths due to infectious and cardiovascular diseases (Weinert & Timiras, 2003; Zweifel, Felder & Meiers, 1999). LE indicators (measured at birth, at 60 years, and at 65 years) may provide further information about the ageing trends.

Regarding the European population median age Eurostat data (Giannakouris, 2008) report a value of 40.4 years in 2008. For 2060 a median age of 47.9 years is estimated.

Over the years, LE has increased considerably. LE at birth in Europe is currently at 79.6 years (min 68 - max 85; WHO 2009), and between 1999 and 2009, LE at birth increased from 76,5 years (73 years for men and 79.6 for women) to 79.6 years (76.7 for

men and 82.6 for women) (Eurostat, 2012). A similar trend is visible in the LE at age 60, when the European population has a mean value of 23.1 years (min. 18.65 – max. 25). In the period between 1999 and 2009 the mean LE at age 60 increased from 20.6 years (18.5 for men and 22.7 for women) to 23.1 years (21.1 for men and 25.1 for women).

Finally, the LE at age 65 is currently 19.1 years (min. 14.25 – max. 21). In 2009 the mean LE at age 65 for men was 17.3 years and 20.9 for women. In 1999 the same index was 14.9 years for men and 18.5 years for women (mean value of 16.7 years, Eurostat, 2012).

The data mentioned above emphasize the magnitude of the demographic change in a very short period of time. It demonstrates the general ageing of European society and how the last phase of life has become longer, resulting in a large increase in the so-called “old elderly” (80 years and over) population (Eurostat, 2012).

These data show a great achievement of contemporary society which, in combination with the amelioration of living conditions and medical progress, allows us to live longer.

2.4 Healthy Life Years

In the next chapters we will elaborate on the concept of healthy life years (HLY). This concept is connected to LE and is defined as the life expectancy in good health.

As will be argued later on, Eurostat data (2012) highlight opposite trends for LE (increasing as highlighted above) and HLY (decreasing). The information derived from Eurostat tables, based on the entire EU population in the period between 2004 and 2010 shows an unhealthy life expectancy at birth of 20 years for women and 15 years for men in 2010, and these values are higher when compared to 2004. A similar trend is observable in the HLY at age 65. From 2004 to 2010, this decreases from 9.7 to 8.8 years (12.1 unhealthy years) for women, and from 9.1 to 8.7 years for men (8.6 unhealthy years).

Data about the HLY are extremely important, because quantification of the healthy life expectancy of European population can serve as the basis for research designs, clinical interventions and sustainable policy actions that aim to increase healthy life expectancy of the aged populations. These actions may result in not just a longer but also a healthier life, with possible positive repercussions on both an individual and a societal level.

2.5 Overview

“Add life to years and not only years to life”; this could be the final statement of this section. In order to maintain or increase quality of life, it is necessary to study the

underlying mechanisms of health in the ageing process and to use these conceptual notions as a springboard to the implementation of preventive interventions. The use of preventive strategies may have an impact on: (i) the individual level, with the reduction of the unhealthy life expectancy, an increase of the autonomy and a consequent reduction of institutionalization rate; (ii) societal level, with a decrease of direct (i.e., hospitalization) and indirect (i.e., loss of quality of life) costs in association with an increase of healthy and active population.

These premises are the basis of the construct of Health-Related Quality of Life (HRQOL), a central topic in the study of the ageing process. The next section addresses HRQOL and will explain its nature and definition.

3. Health-Related Quality of Life

Health-related topics are relevant on an individual and societal level due to the current demographic changes and how society is ageing. This study deals with health-related topics during the ageing process using the construct of Health-Related Quality of Life (HRQOL).

3.1 Definition and background

3.1.1 Health and health models

Health was defined by WHO (1948) as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”. This definition was revolutionary because it reversed the classical point of view; it conceptualized health in a positive way, focusing not on diseases or limitations, but on well-being. Additionally it proposes a multidimensional construct of health, including physical, mental and social determinants, stating that a complete state of health must concern the well-being in each of these domains, and not only in physical-biological aspects.

The biopsychosocial model was developed using the definition of health as a starting point (Engel, 1977). This model defined health as continuum trend-line (from worst to best possible health). The biopsychosocial model is in contrast with the classical biomedical model, in which the categories “health” and “infirmity” are on opposite sides of spectrum. Furthermore, the biopsychosocial model considers interconnections and mutual influences among health domains, with the use of a systemic approach, based on systems theory (Engel, 1977). Conversely, the biomedical model adopts a mechanistic and reductionist approach, allowing only linear and causal relationships from a lower level (biological functions) to a higher level (general health; Engel, 1977).

The biopsychosocial model made the study of health and health-related topics as systems of interconnected elements that may vary and change over time in a continuous way possible. The biopsychosocial model represents the basis of this thesis.

Engel's model (1977) was applied in many areas of research and clinical practice, and it has a wide impact and visibility (Engel's article has currently been cited 6754 times). However, despite the innovative and interesting conceptualization, recent findings (Fava & Sonino, 2008; White, 2005) affirm that, thirty years after its conceptualization, the biopsychosocial model has not yet seen any large-scale integration; despite its limitations, the biomedical model continues to be the model most often used.

This thesis applies Engel's model to the construct on HRQOL together with a Dynamic Systems approach, pursuing the following objectives: (i), to re-conceptualize the construct and, (ii) to create a theoretical and applicable framework for the expansion of the use of the biopsychosocial model in clinical practice.

3.1.2 Quality of Life and HRQOL

The construct of HRQOL is the central topic of this thesis. To start with, we will provide a general background on the concepts of Quality of Life (QOL) and HRQOL, for a better conceptual framework.

The emergence and use of the QOL concept derives from the scarce information provided by indicators of morbidity and mortality (Idler & Benyamini, 1997). QOL is a person-centered measure, which includes the individual perception of life within a context and in relation to personal goals and expectations (WHO, 1997). Over the years, a large consensus has been reached concerning the concept of QOL, with an increasing number of published articles. A basic search of the key phrase "quality of life" results in 179,742 hits, with a minimum number of published articles in between 1959 and 1964 ($n = 1$) and a maximum in 2012 ($n = 15,330$). The trend line of published papers found in PubMed is presented in Figure 1.

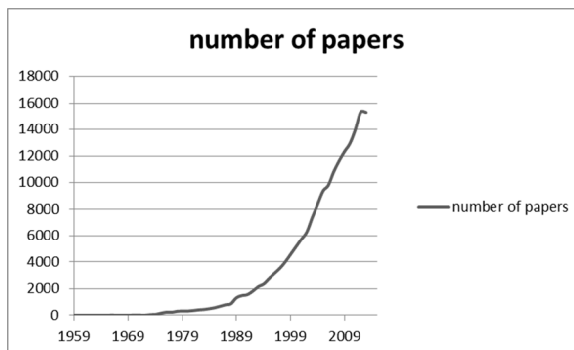


Figure 1 - Number of papers on QOL

However, despite the large number of QOL studies, this construct remains “an amorphous concept, that is used in many disciplines – geography, literature, health economics, advertising, health promotion and medical and social science” (Bowling, 1999). One of the most important and common problems concerning QOL is that it is an umbrella term, in which, theoretically, all the aspects of life are included (Bowling, 1999). Because the construct is so broad, it is difficult to operationalize and measure (because it may have different meanings in different fields of interest (cf. Farquhar, 1995; Hunt, 1997).

The concept of HRQOL was developed in order to make QOL less broad. HRQOL is based on the perceived impact of the health status (Testa & Simonson, 1996). HRQOL narrows the focus to the physical, mental and social domains of health, that are seen as aspects that can be influenced by intra- and interindividual influences. Furthermore, aspects of QOL such as cultural, societal or political factors, which are not included in the definition of health, are excluded from the concept of HRQOL (Ferrans, Zerwic, Wilbur, & Larson, 2005).

HRQOL was defined as a personal and dynamic concept, because it is a self-evaluation of health and an internal process which may be influenced by complex interactions of factors (Allison, Locker & Feine, 1997; Bastani & Kiadaliri, 2011; Dempster & Donnelly, 2000; Morris, Suissa, Sherwood, Wright & Greer, 1986). Although HRQOL is thus seen as a dynamic concept, research mainly addresses it in a static manner.

HRQOL is a useful concept to study how processes act on a person and predictions of negative health outcomes (Theofilou, 2011). Specifically, on the one hand HRQOL measures are used to test the effectiveness of interventions (as an example: Sillanpää, Häkkinen, Holviala, & Häkkinen, 2012) and diseases (cf. Lam & Lauder, 2000). In order to understand whether changes in HRQOL reflect clinically meaningful differences as well, statistically based methods were developed (Crosby, Kolotkin & Williams, 2003). These methods aim to identify the smallest possible changes in HRQOL that reflect a change in clinical differences and patient management. On the other hand, especially in older adults, measures of HRQOL are used as indicators of negative health outcomes (cf. Dominick, Ahern, Gold, & Heller, 2002; Tsai, Chi, Lee, & Chou, 2007).

Finally, HRQOL measures may be useful for national and supranational policy makers in order to understand whether health-related objectives are being reached and to implement substantial and efficient strategies to enhance the general standard of health and perceptions of individuals (Theofilou, 2011).

4. Overview of the thesis

4.1 General aim

Despite the important role of HRQOL as an outcome and predictor measure, there currently are still some gaps in the conceptualization and measurement of the construct. From a conceptual point of view, a great number of conceptual models have been developed resulting in a high number of instruments, with a low coherence. Furthermore, the most generally adopted conceptual models are based on a biomedical approach (Wilson & Cleary, 1995), while an approach based on the biopsychosocial model may result in a better comprehension of the construct. From an applicable point of view, studies that reported how HRQOL develops during time and how the different domains are related to each other during time are lacking.

Especially these two topics – the development over time and the interrelations between domains – need further study, because insight into these topics may result in a better understanding of the nature and development of HRQOL, with possible interesting applicable solutions in the area of health promotion and prevention of negative health outcomes during the ageing process.

The general aim of the thesis is to apply a Dynamic Systems approach to the construct of HRQOL, with the possibility to expand the conceptualization of the construct and to analyze dynamic trends and characteristics over time in older adults.

4.2 Structure

This thesis is a collection of papers. Specifically, three papers are included in the thesis. They cover the general aim of the thesis, starting with a conceptual study and arriving at an empirical investigation. Each paper follows the previous one, and the entire thesis creates a kind of framework in which the construct of HRQOL is studied using a Dynamic Systems approach. Each paper represents a chapter of the thesis.

The aim of the second chapter is to present a conceptual model of HRQOL based on Dynamic Systems theory. To do so, after a first look at demographical trends and age-related health changes, the chapter focuses on existing models of HRQOL, as we try to find common points and current limitations. Furthermore, similarities between HRQOL and Dynamic Systems are presented as well as a conceptual model that meets all the cited requirements is. Next, the operationalization of the model is presented, in order to give an applicable translation of the conceptual assumptions. Finally, possible developments as well as limitations of the model are presented.

The third chapter is connected to the second one, and in particular aims to analyze the validity of the conceptual model through the construction and validation of a mathematical dynamic systems model that represents the conceptual model. In this chapter, the connections and the theoretical assumptions made in the previous chapter are translated into a numerical form by the application of non-linear equations as generally used in Dynamic Systems modeling. The construction of this model is a necessary step in order to analyze the ability of the conceptual model to catch salient information of HRQOL. To test this ability, the mathematical model is tested by means of a twofold procedure with empirical data. Results show a good fit of the mathematical model with these data. Because the model is developed to represent the theory, and not just to describe variations in a data set, such as Structural Equation Models, this fit strongly indicates that the theoretical model is satisfactory. Additionally, this chapter presents possible further research and applications, as well as current limitations.

Finally, the fourth chapter, using the theoretical basis developed in the conceptual model as a starting point, analyzes daily trends of HRQOL in a small sample of institutionalized older adults.

In chapter three, we found evidence for the validity of our assumption that development of HRQOL can be viewed as a dynamic system. The perception of HRQOL as a dynamic system that changes over time opens new possibilities for research. An important characteristic in dynamic behavior, which reveals much information about the process, is variability, and especially the changes in variability over time. For that reason, in chapter four we investigate whether and how patterns of variability can provide relevant information about the development of HRQOL in individuals. Chapter four argues that the participants show dynamic and unstable daily HRQOL sequences during the research project (100 days) and it is demonstrated that day-to-day variability is related to health trends and final state. By starting from variations in intra individual data sets, this chapter is an attempt to study HRQOL from a Dynamic Systems perspective. The results seem to confirm our theoretical expectations, even if, especially in this case, extreme caution must be taken in the data handling, since the sample size is very limited.

At the end of the three main chapters, a general conclusion is presented, with the aim to summarize the work, the principal results, applicable solutions and further steps that must be addressed. Aims, methods, results and conclusions for each study are summarized in Table 1.

Chapter 1 - Introduction

Chapter 2	Older adults and Health Related Quality of Life: a conceptual model based on a dynamic systems perspective
Aims	<ol style="list-style-type: none"> 1. To discuss if the construct of HRQOL may be associated and conceptualized with a dynamic systems approach 2. To present a new conceptual model of HRQOL in the aged population, based on dynamic systems theory
Methods	This is a conceptual study. The concept of HRQOL was analyzed in light of a dynamic systems approach. Furthermore, a conceptual model was designed including salient characteristics and their relations during time
Results	<ol style="list-style-type: none"> 1. HRQOL seems to fit within the dynamic systems framework 2. An operational definition of the conceptual model was delineated, in order to allow further development and tests
Conclusion	<ol style="list-style-type: none"> 1. The conceptual model can provide new ideas and insights about the processes acting in the ageing period, due to the use of developmental view and dynamic systems approach 2. Further empirical studies are necessary to confirm these assumptions
Chapter 3	A quantitative Dynamic Systems model of Health Related Quality of Life among older adults
Aims	<ol style="list-style-type: none"> 1. To translate the conceptual model in a mathematical one 2. To test the goodness of the model by a calibration and a validation procedure
Methods	<ol style="list-style-type: none"> 1. The model building is made by translating the components of the model in a numerical form and by assigning non-linear equations to each directed relationship presented in the conceptual model (arrows in the graphical model) 2. The calibration procedure was made with theoretically plausible data in order to assess how the model reacts to different initial sets of data 3. Empirical data of 194 community dwelling older-adults are used as initial and outcome data to validate the model
Results	<ol style="list-style-type: none"> 1. The calibration procedure detects the parameter ranges within the model reacts with theoretically acceptable trends 2. The model fits empirical data in a satisfactory way, showing no statistically or conceptually meaningful differences between empirical and simulated final data
Conclusion	<ol style="list-style-type: none"> 1. The validation procedure returns positive results in agreement with theoretical expectations 2. Data suggests the goodness of theoretical assumptions about the dynamic development of HRQOL in the aged population
Chapter 4	"How I feel today?" An analysis of HRQOL variability among institutionalized older adults
Aims	<ol style="list-style-type: none"> 1. To test how the construct of HRQOL develops during time among older-adults 2. To analyze if indicators of variability are related with developmental trends and final health outcomes
Methods	<ol style="list-style-type: none"> 1. 22 institutionalized older-adults participated in the longitudinal design study 2. Participants fill out daily and monthly questionnaire measures of HRQOL 3. Data analyses are conducted to find reliability and construct validity of daily measures 4. Day-to-day variability is computed and related to health outcomes and trends 5. Day-to-day variability before an extreme value in the developmental trends is compared with day-to-day variability in the whole period
Results	<ol style="list-style-type: none"> 1. Daily measures are correlated with monthly validated questionnaires 2. Day-to-day variability is generally related with negative health outcomes and trends 3. Variability preceding an extreme value in the developmental trends, is higher than day-to-day variability in the whole period
Conclusion	<ol style="list-style-type: none"> 1. The role of daily variability emerges as an important indicator of final outcomes and developmental trends 2. Data suggest that HRQOL may present typical characteristics of dynamic systems, however, due to the small sample size, these data need to be confirmed by other studies

Table 1 - The thesis at a glance

5. References

- Allison, P. J., Locker, D., & Feine, J. S. (1997). Quality of life: A dynamic construct. *Social Science & Medicine*, 45(2), 221–230. doi:10.1016/S0277-9536(96)00339-5
- Bastani, P., & Kiadaliri, A. A. (2011). Health-related quality of life after chemotherapy cycle in breast cancer in Iran. *Medical Oncology*, 28(1), 70–74. doi:10.1007/s12032-010-9714-x
- Bowling, A. (1999, September). Health-Related Quality of Life: a discussion of the concept, its use and measurement.
- Crosby, R. D., Kolotkin, R. L., & Williams, G. R. (2003). Defining clinically meaningful change in health-related quality of life. *Journal of Clinical Epidemiology*, 56(5), 395–407. doi:10.1016/S0895-4356(03)00044-1
- Dempster, M., & Donnelly, M. (2000). How well do elderly people complete individualised quality of life measures: An exploratory study. *Quality of Life Research*, 9(4), 369–375. doi:10.1023/A:1008959925664
- Dominick, K., Ahern, F., Gold, C., & Heller, D. (2002). Relationship of health-related quality of life to health care utilization and mortality among older adults. *Aging clinical and experimental research*, 14(6), 499–508.
- Engel, G. L. (1977). The need for a new medical model: a challenge for biomedicine. *Science*, 196(4286), 129–136. doi:10.1126/science.847460
- European Commission. (2012). *Active ageing and solidarity between generations. A statistical portrait of the European Union 2012* (Vol. 1). Luxembourg: Office for Official Publ. of the European Communities.
- Farquhar, M. (1995). Definitions of quality of life: a taxonomy. *Journal of Advanced Nursing*, 22(3), 502–508. doi:10.1046/j.1365-2648.1995.22030502.x
- Fava, G. A., & Sonino, N. (2008). The Biopsychosocial Model Thirty Years Later. *Psychotherapy and Psychosomatics*, 77(1), 1–2. doi:10.1159/000110052
- Ferrans, C. E., Zerwic, J. J., Wilbur, J. E., & Larson, J. L. (2005). Conceptual Model of Health-Related Quality of Life. *Journal of Nursing Scholarship*, 37(4), 336–342. doi:10.1111/j.1547-5069.2005.00058.x
- Franceschi, C., Valensin, S., Bonafè, M., Paolisso, G., Yashin, A. ., Monti, D., & De Benedictis, G. (2000). The network and the remodeling theories of aging: historical background and new perspectives. *Experimental Gerontology*, 35(6–7), 879–896. doi:10.1016/S0531-5565(00)00172-8

Giannakouris, K. (2008). Population and social conditions. Ageing characteristics the demographic perspectives of the European societies. Eurostat, Statistic in focus.

Hickey, D. A., Barker, M., McGee, H., & O'Boyle, C. (2005). Measuring health-related quality of life in older patient populations. *Pharmacoeconomics*, 23(10), 971–993. doi:10.2165/00019053-200523100-00002

Hunt, S. M. (1997). The problem of quality of life. *Quality of Life Research*, 6(3), 0–0. doi:10.1023/A:1026402519847

Idler, E. L., & Benyamini, Y. (1997). Self-Rated Health and Mortality: A Review of Twenty-Seven Community Studies. *Journal of Health and Social Behavior*, 38(1), 21–37. doi:10.2307/2955359

Kirkwood, T. B. . (2002). Evolution of ageing. *Mechanisms of Ageing and Development*, 123(7), 737–745. doi:10.1016/S0047-6374(01)00419-5

Kirkwood, T. B. L., & Kowald, A. (1997). Network theory of aging. *Experimental Gerontology*, 32(4–5), 395–399. doi:10.1016/S0531-5565(96)00171-4

Lam, C. L., & Lauder, I. J. (2000). The impact of chronic diseases on the health-related quality of life (HRQOL) of Chinese patients in primary care. *Family Practice*, 17(2), 159–166. doi:10.1093/fampra/17.2.159

Morris, J. N., Suissa, S., Sherwood, S., Wright, S. M., & Greer, D. (1986). Last days: A study of the quality of life of terminally ill cancer patients. *Journal of Chronic Diseases*, 39(1), 47–62. doi:10.1016/0021-9681(86)90106-2

Pollack, M. E. (2005). Intelligent Technology for an Aging Population: The Use of AI to Assist Elders with Cognitive Impairment. *AI Magazine*, 26(2), 9. doi:10.1609/aimag.v26i2.1810

Sillanpää, E., Häkkinen, K., Holviala, J., & Häkkinen, A. (2012). Combined Strength and Endurance Training Improves Health-Related Quality of Life in Healthy Middle-Aged and Older Adults. *International Journal of Sports Medicine*, 33(12), 981–986. doi:10.1055/s-0032-1311589

Testa, M. A., & Simonson, D. C. (1996). Assessment of Quality-of-Life Outcomes. *New England Journal of Medicine*, 334(13), 835–840. doi:10.1056/NEJM199603283341306

Theofilou, P. (2011). Why is it Important to Assess Health - Related Quality of Life? *Journal of Palliative Care & Medicine*, 01(01). doi:10.4172/2165-7386.1000e104

Tsai, S.-Y., Chi, L.-Y., Lee, C., & Chou, P. (2007). Health-related quality of life as a predictor of mortality among community-dwelling older persons. *European Journal of Epidemiology*, 22(1), 19–26. doi:10.1007/s10654-006-9092-z

Chapter 1 - Introduction

Weinert, B. T., & Timiras, P. S. (2003). Invited Review: Theories of aging. *Journal of Applied Physiology*, 95(4), 1706–1716. doi:10.1152/jappphysiol.00288.2003

White, P. (2005). *Biopsychosocial Medicine: An Integrated Approach to Understanding Illness*. Oxford University Press.

Wilson, I., & Cleary, P. (1995). Linking clinical variables with health-related quality of life: A conceptual model of patient outcomes. *JAMA*, 273(1), 59–65. doi:10.1001/jama.1995.03520250075037

World Health Organization. (1997). *WHOQOL, measuring Quality of Life; division of mental health and prevention of substance abuse* (No. WHO/MSA/MNH/PSF/97.4) (p. 15). Geneva: WHO.

Zweifel, P., Felder, S., & Meiers, M. (1999). Ageing of population and health care expenditure: a red herring? *Health Economics*, 8(6), 485–496. doi:10.1002/(SICI)1099-1050(199909)8:6<485::AID-HEC461>3.0.CO;2-4